UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,835	03/22/2001	Neil Stahl	REG 203B-US	8053

7590 08/30/2004

Linda O Palladino
Regeneron Pharmaceuticals Inc
777 Old Saw Mill River Road
Tarrytown, NY 10591

EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,835	STAHL ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,10-19,25,26 and 29-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10-19,25,26 and 29-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 March 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-3, 10-19, 25, 26 and 29-35 are pending in the instant application. Claims 1-3, 10, 12, 13, 15, 16, 19 and 26 have been amended, claims 4-9, 20-24, 27 and 28 have been canceled and claims 29-35 have been added as requested by Applicant in the Paper filed August 21, 2003.

Election/Restrictions

2. Applicant's election of species of cytokine trap directed to interleukin-18 in the reply filed on August 21, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

All pending claims will be examined on the merits.

Specification

3.2 The abstract of the disclosure is objected to because it is from the wrong PCT application (PCT/US99/22253, instead of PCTUS99/22045). Correction is required. See MPEP § 608.01(b).

3.2 The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Receptor based antagonists of IL-18.

Drawings

4. Figures 4 and 9 of the instant application are presented on 2 separate panels. 37 C.F.R. § 1.84(U)(1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, they must be identified by the same number followed by a capital letter. For example, Figure 4 is labeled on the first sheet as Fig. 4 and the second sheet as Fig. 4 (Cont). The same is the case for Figure 9. The other drawings containing multiple sheets of continued sequences are labeled correctly. It is acknowledged that the amendment filed August 6, 2002, amended the specification to recite in the legends on pages 6 and 8 FIGURES 4A-4B and FIGURES 9A-9B, but the drawings must be corrected to meet the separate numbering requirement of 37 C.F.R. § 1.84(U)(1).

Priority Determination

35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

5. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. The instant claims are drawn to fusion proteins comprising IL-18 receptors. Applications 60/101,858 and 09/313,942, teach fusion proteins comprising receptors to a number of cytokines, but not to IL-18. Therefore, those applications do not meet the written description guidelines for fusion proteins comprising IL-18 receptors, and are unavailable under 35 U.S.C. § 120 or § 119(e), and the effective priority date of the instant application is considered to be the filing date of PCT/US99/22045, Sept. 22, 1999.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6.1 Claims 1-3, 10-19, 25, 26 and 29-35 are rejected under 35 U.S.C. 102(a) as being anticipated by Sims et al, WO 99/37772, July 29, 1999 (cited by Applicants).

Claims 1-3, 10-19, 25, 26 and 29-35 encompass fusion polypeptides comprising a first component comprising an amino acid sequence of an IL-18 binding portion of an extracellular domain of a specificity determining component of an IL-18 receptor, a second component comprising an amino acid sequence of an IL-18 binding portion of an extracellular domain of a

signal transducing component of an IL-18 receptor, and a third component comprising the amino acid sequence of a multimerizing component, wherein the multimerizing component comprises an immunoglobulin domain which may be Fc domain of IgG, the heavy chain of IgG or the light chain of IgG, composition capable of binding IL-18 to form a nonfunctional complex comprising a multimer or dimer of the fusion polypeptide, nucleic acids encoding the fusion polypeptides wherein the nucleic acid sequence encoding the first component is upstream or is downstream of the nucleotide sequence encoding the second component, vectors, host cells which may be bacterial, yeast, insect or mammalian, *E. coli*, COS or CHO, recombinant method of making the fusion polypeptide and compositions comprising fusion proteins that bind IL-18.

Sims et al. teaches heteromeric receptor complexs that bind IL-18. Sims et al. teaches that IL-1Rrp1 binds IL-18 only weakly and mediates signaling in transfected cells and that AcPL does not bind IL-18, but that a complex of IL-1Rrp1 and AcPL results in a dramatic enhancement of signaling in cells stimulated with IL-18 (page 2, lines 10 to 41). Sims et al. teach that dimeric IL-18 receptor complexes comprising IL-1Rrp1 and AcPL or fragments thereof can be useful for inhibiting IL-18 activity, that IL-1Rrp1 and AcPL receptor subunits may be covalently linked by a polypeptide linker to make fusion proteins, that AcPL/IL-1RrP1 dimers can be prepared by fusing one of the receptor subunits to the constant region of an immunoglobulin chain and fusing the other receptor to the constant region of an immunoglobulin light chain, and that cells transfected with the DNA encoding these fusion proteins can produce these heterodimers to form multimers (page 3, lines 1-26). Sims et al. teach that recombinant fusion proteins can be constructed with the C-terminal portion of AcPL fused to the N-terminal portion of IL-1Rrp1, or constructed with the C-terminal portion IL-1Rrp1of fused to the N-

terminal portion of AcPL (nucleic acids encoding the fusion polypeptides wherein the nucleic acid sequence encoding the first component is upstream or is downstream of the nucleotide sequence encoding the second component) (pages 11, line 18 to page 12, line 26), expression vectors, host cells which may be bacterial, yeast, insect or mammalian, *E. coli*, COS or CHO, recombinant method of making fusion polypeptides (page 12, line 27 to page 16, line 37), and compositions comprising fusion proteins which are useful as IL-18 binding agents (page 21, line 37 to page 22, line 39, also see claims). Therefore, Sims et al. anticipates the claims.

6.2 Claims 1-3, 10-19, 25, 26 and 29-35 are also rejected under 35 U.S.C. 102(e) as being anticipated by Sims et al., U.S. Patent No. 6,589,764, effective priority date January 22, 1999.

Sims et al. teaches heteromeric receptor complexs that bind IL-18. Sims et al. teaches that IL-1Rrp1 binds IL-18 only weakly and mediates signaling in transfected cells and that AcPL does not bind IL-18, but that a complex of IL-1Rrp1 and AcPL results in a dramatic enhancement of signaling in cells stimulated with IL-18. Sims et al. teach that dimeric IL-18 receptor complexes comprising IL-1Rrp1 and AcPL or fragments thereof can be useful for inhibiting IL-18 activity, that IL-1Rrp1 and AcPL receptor subunits may be covalently linked by a polypeptide linker (fusion protein), that AcPL/IL-1RrP1 dimers can be prepared by fusing one of the receptor subunits to the constant region of an immunoglobulin chain and fusing the other receptor to the constant region of an immunoglobulin light chain, that cells transfected with the DNA encoding these fusion proteins can produce these heterodimers to form multimers (column 2, line 10 to column 4, line 11). Sims et al. teach that recombinant fusion proteins can be constructed with the C-terminal portion of AcPL fused to the N-terminal portion of IL-1Rrp1, or constructed with the C-terminal portion IL-1Rrp1of fused to the N-terminal portion of AcPL

(nucleic acids encoding the fusion polypeptides wherein the nucleic acid sequence encoding the first component is upstream or is downstream of the nucleotide sequence encoding the second component), expression vectors, host cells which may be bacterial, yeast, insect or mammalian, *E. coli*, COS or CHO, recombinant method of making fusion polypeptides (column 9, line 25 to column 13, line 54), and compositions comprising fusion proteins which are useful as IL-18 binding agents (column 17, line 46 to column 18, line 55, also see claims). Therefore, Sims et al. anticipates the claims.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.ispto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner

Eileen B. O'Hara

EILEEN B. O'HARA
PATENT EXAMINER